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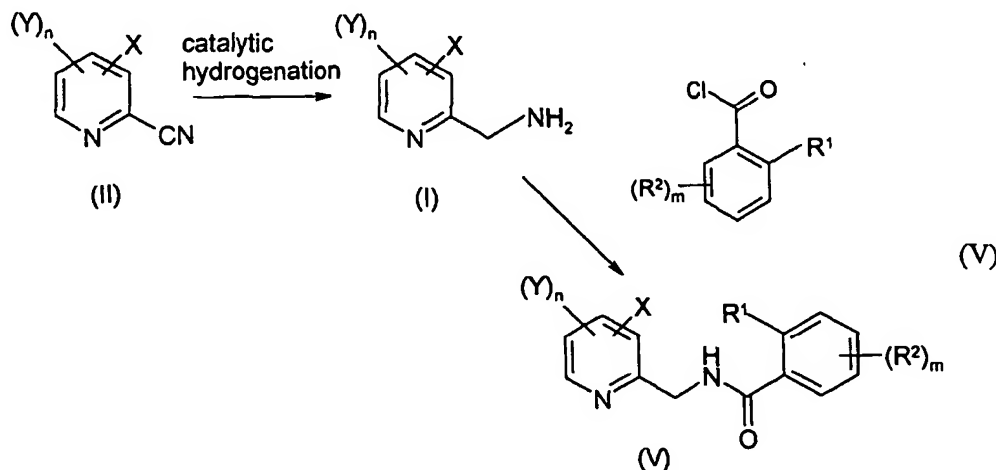
(43) International Publication Date  
28 February 2002 (28.02.2002)

PCT

(10) International Publication Number  
**WO 02/16322 A2**

- (51) International Patent Classification<sup>7</sup>: C07D 213/00 (74) Agents: TETAZ, Franck et al.; Aventis CropScience S.A., Dépt. Propriété Industrielle, B.P. 9163, 14-20, rue Pierre Baizet, F-69263 Lyon Cedex 09 (FR).
- (21) International Application Number: PCT/EP01/10984
- (22) International Filing Date: 21 August 2001 (21.08.2001) (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:  
0021066.6 25 August 2000 (25.08.2000) GB  
0025616.4 19 October 2000 (19.10.2000) GB  
01420128.9 7 June 2001 (07.06.2001) EP
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- (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:  
— without international search report and to be republished upon receipt of that report
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: NOVEL PROCESS



(57) Abstract: The invention relates to a process for the preparation of a compound of formula (V), according to the following scheme: wherein the various substituents are as defined in the description.

### NOVEL PROCESS

5 [0001] This invention relates to novel processes for the preparation of 2-aminomethylpyridines (particularly 2-aminomethyl-3-chloro-5-trifluoromethylpyridine), and for the preparation of 2-cyanopyridines used in their preparation, which compounds are useful as intermediates for the production of pesticides.

10

[0002] The catalytic reduction of cyanopyridines to give aminomethylpyridines is known. However when the cyanopyridine compound contain additional halogen atom(s) the reduction may be complicated by the competing dehalogenation reaction. It is stated by P. N. Rylander, *Hydrogenation Methods* (Best Synthetic Series, published by Academic Press), (1985), page 148, that palladium is usually  
15 the catalyst of choice when wishing to effect a dehalogenation reaction, and that platinum and rhodium are relatively ineffective and are hence often used in hydrogenations where the halogen is to be preserved.

20 [0003] In contrast with the above prior art teaching we have found that the use of a palladium catalyst gives particularly good results in the reduction of cyanopyridines which contain additional halogen atom(s). We have developed a new process for the preparation of 2-aminomethylpyridines, which contain additional halogen atom(s) in which minimal dehalogenation occurs, and which is  
25 applicable to industrial scale processes.

[0004] There have been a number of procedures published for introducing a cyano group at the 2-position of a pyridine moiety. These typically involve substitution of a halogen, in particular bromine or fluorine, in a polar solvent, e.g. dimethyl  
30 sulphoxide or dimethylformamide. In addition, there are numerous methods

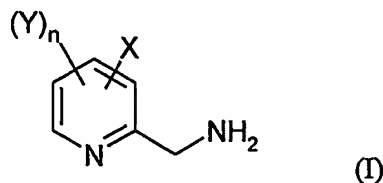
starting from the activated pyridine *N*-oxide or *N*-alkylpyridine. Many of these cyanation routes use heavy metal reagents, containing copper or nickel. For example, EP0034917 discloses the preparation of 2-cyano-3-chloro-5-trifluoromethylpyridine from the 2-bromo analogue by reaction with cuprous  
5 cyanide in dimethylformamide at 120°C.

[0005] However, many of these prior art processes suffer from one or more drawbacks, including poor yields, use of heavy metals which produce toxic effluents, or polar solvents which are difficult to recover. Further, methods which  
10 involve formation of the pyridine *N*-oxide or *N*-alkylpyridine involve several steps. These drawbacks are more critical on scale-up to industrial scale.

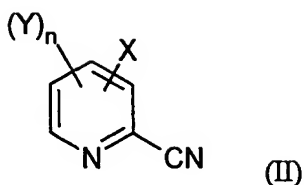
[0006] GB Patent Publication Number 117970 describes the cyanation of 2-halopyridine compounds with an activating agent and a cyanide source in a  
15 polar solvent and thus avoids many of the above disadvantages. However there still remains with this procedure the need to recycle the activating agent and the aprotic solvent in order to minimise the costs for an industrial scale process.

[0007] We have now developed an alternative and improved process for the  
20 preparation of 2-cyanopyridines which is applicable to industrial scale processes.

[0008] According to a first aspect of the present invention, there is provided a process (A) for the preparation of a compound of general formula (I):



25 or a salt thereof, which process comprises the catalytic hydrogenation of a compound of general formula (II):



or a salt thereof,

wherein X is halogen; each Y, which may be the same or different, is halogen,

5 haloalkyl, alkoxy carbonyl or alkylsulphonyl; and n is 0 to 3.

[0009] In this invention halogen means a fluorine, chlorine or bromine atom. The preferred halogen atom is chlorine.

10 [0010] Haloalkyl typically means a C<sub>1</sub> to C<sub>6</sub> alkyl moiety substituted by one or more halogen atoms. For example the C<sub>1</sub> to C<sub>6</sub> alkyl moiety may be methyl, ethyl, n-propyl or i-propyl, preferably methyl. The C<sub>1</sub> to C<sub>6</sub> alkyl moiety is preferably substituted by one or more chlorine or fluorine atoms. A more preferred haloalkyl group is trifluoromethyl.

15

[0011] An alkoxy carbonyl group is typically C<sub>1</sub> to C<sub>6</sub> alkoxy carbonyl such as methoxy carbonyl, ethoxy carbonyl, n-propoxy carbonyl or i-propoxy carbonyl.

[0012] An alkylsulphonyl group is typically C<sub>1</sub> to C<sub>6</sub> alkylsulphonyl in which the  
20 C<sub>1</sub> to C<sub>6</sub> moiety is as defined above.

[0013] Preferably X is chlorine.

[0014] Preferably Y is halogen or haloalkyl (more preferably trifluoromethyl).

25

[0015] Compound (II) is preferably 3-chloro-2-cyano-5-trifluoromethylpyridine.

[0016] The catalyst generally comprises a metal selected from palladium, platinum, ruthenium, nickel and cobalt. The amount of metal in the catalyst used (which is generally supported on for example charcoal) is generally from 0.05-0.7% by weight relative to the amount of the compound of formula (II), preferably  
5 from 0.05-0.3%, more preferably from 0.1-0.2%. A preferred catalyst contains palladium, for example finely divided palladium on an inert carrier such as charcoal. This has been found to give both a convenient reaction rate and minimal side reactions. Thus when the compound of formula (II) is 3-chloro-2-cyano-5-trifluoromethylpyridine, minimal dechlorination occurs when using the process of  
10 the invention. Other examples of suitable catalysts include catalysts comprising oxides or other compounds of the above mentioned metals.

[0017] The process is typically carried out in the presence of a solvent such as an alcohol, for example methanol, ethanol, propanol or butanol, or an ester such as  
15 ethyl acetate, or an ether such as tetrahydrofuran. Alcohol solvents are preferred (methanol is most preferred). The process is preferably performed in the presence of a strong acid such as hydrochloric acid, hydrobromic acid, sulphuric acid or phosphoric acid (preferably hydrochloric acid). The presence of the acid helps prevent poisoning of the catalyst by the amino group of the product of formula (I),  
20 and also prevents the coupling of amino intermediates which is otherwise known to occur during the catalytic hydrogenation of nitriles.

[0018] The reaction conditions typically comprise combining all reactants in a suitable reaction vessel and stirring, for example at a temperature of from 0 to  
25 60°C, preferably from 20 to 30°C. A further advantage of the process is that low pressures are used, with a hydrogen pressure of from 1 to 4 atmospheres generally being employed (the process is preferably performed at 1 atmosphere).

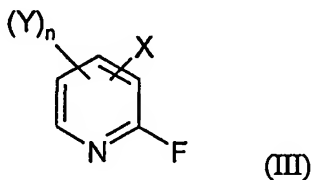
[0019] The reaction is optionally performed in the presence of a catalyst inhibitor,  
30 which can lead to a further improvement in the reaction selectivity by reducing the

amount of dehalogenation which may occur as a side reaction. Such catalyst inhibitors are known in the art, for example as described in P.N.Rylander in *Hydrogenation Methods (Best Synthetic Series, published by Academic Press)*, 1985, pages 125-126, and include alkali metal bromides or iodides such as potassium bromide and potassium iodide; or ammonium bromide or ammonium iodide; or hydrogen bromide or hydrogen iodide; or phosphorus compounds such as triphenyl phosphite, hypophosphorous acid, phosphorous acid or alkylphosphinic acids; or thiodiglycol (2,2'-thiodiethanol); or thiourea; or sulphur. Preferably the catalyst inhibitor is selected from an alkali metal bromide or iodide, ammonium bromide or iodide and hydrogen iodide.

[0020] The present invention thus provides a high yielding, selective and convenient process for the preparation of 2-aminomethylpyridines .

[0021] It is particularly convenient to generate the compound of formula (I) in the form of a salt, especially a hydrochloride salt. When used as an intermediate in the production of a pesticide the salt can be submitted directly to the next reaction step without prior isolation of the corresponding free amine. The production of the salt and its subsequent reaction can therefore be conveniently carried out in a single vessel. A particularly preferred salt is 2-aminomethyl-3-chloro-5-trifluoromethylpyridine hydrochloride.

[0022] According to a further feature of the present invention, there is provided a process (B) for the preparation of a compound of general formula (II) as defined above which comprises treating a compound of general formula (III):



with a cyanide source and a catalyst in an aqueous solvent or without solvent,

wherein X, Y and n are as hereinbefore defined; and wherein the cyanide source is hydrogen cyanide, an alkali metal cyanide, an alkaline earth metal cyanide or an optionally substituted ammonium cyanide.

[0023] The catalyst is generally a phase transfer catalyst such as a tetraalkyl ammonium salt such as benzyl trimethylammonium chloride, tricapyrylmethylammonium chloride, tetramethylammonium chloride, tetra-n-propylammonium bromide, n-dodecyl trimethylammonium chloride, tetra-n-butylammonium chloride, tetra-n-butylammonium bromide, tetra-n-octylammonium bromide or n-tetradecyl trimethylammonium bromide; or a tetraalkyl phosphonium salt such as tetra-n-butylphosphonium bromide or tetraphenylphosphonium bromide; or a crown ether or acyclic analogue thereof such as TDA-1 (tris[2-(2-methoxyethoxy)ethyl]amine); or an amine such as 4-dimethylaminopyridine.

[0024] Preferably the catalyst is selected from tricapyrylmethylammonium chloride and tetra-n-octylammonium bromide.

[0025] The amount of catalyst used is generally from about 0.01 to 10 mol %, preferably from about 0.1 to 5 mol %, more preferably from about 1 to 5 mol %.

[0026] Compound (III) is preferably 3-chloro-2-fluoro-5-trifluoromethylpyridine.

[0027] The above process (B) of the invention is a high yielding process for the preparation of 2-cyanopyridines, which is simple to perform and operates at moderate temperatures and does not suffer from the drawbacks of many prior art processes. In particular the process of the invention does not require heavy metal cyanides such as copper or nickel cyanide, which, when used on an industrial

scale, produce toxic effluent streams and are difficult to recover. The process (B) of the invention produces waste streams, which are readily treatable.

[0028] In addition, the process does not require the preparation of activated  
5 pyridine *N*-oxide or *N*-alkylpyridine for high conversions, which is a requisite for many of the prior art processes. The process (B) of the invention does not require an activating agent such as 4-dimethylaminopyridine and hence avoids additional recovery and recycling steps. A further advantage of the process (B) of the  
10 invention is that organic solvents are not used in the reaction, thus avoiding the need to recycle expensive solvents such as dimethyl sulphoxide.

[0029] The cyanide source is preferably sodium cyanide or potassium cyanide, preferably potassium cyanide. The amount of cyanide source used is generally from about 1.0 to about 2.0 molar equivalents (however more may be used if  
15 desired), preferably from 1.0 to 1.5 molar equivalents, more preferably from 1.0 to 1.1 molar equivalents.

[0030] The reaction is generally and preferably performed using water as solvent, however it may also be carried out in the absence of solvent.  
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[0031] The reaction conditions typically comprise combining all reactants in a suitable reaction vessel and stirring at a temperature of from 10 to 60°C, preferably from 20 to 40°C.

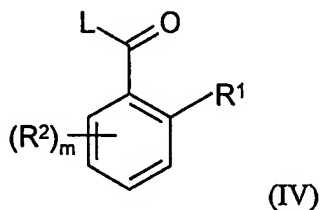
[0032] The present invention thus provides a high yielding process (B) for the  
25 preparation of 2-cyanopyridines. Since the reaction uses moderate reaction temperatures, simple and inexpensive reactors and downstream processing equipment is all that is required. Furthermore, since the reactants are readily available, the process is inexpensive to operate. In addition, the present process  
30 produces waste streams that are readily treatable.



[0033] According to a further feature of the invention the processes (B) and (A) can be combined to prepare a compound of formula (I) from a compound of formula (III).

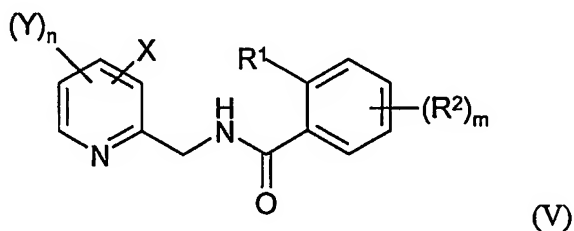
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[0034] According to a further feature of the invention the process (A), or the combined processes (B) and (A), is followed by a further process step (C) which comprises the acylation of said compound (I) with a benzoyl compound of formula (IV):



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wherein L is a leaving group; R<sup>1</sup> and R<sup>2</sup> each represent the same or different halogen; and m is 0, 1 or 2, to give a compound of formula (V):



15

[0035] Preferably L is chlorine.

[0036] Compounds of Formula (V) are valuable pesticide active ingredients disclosed for example in International Patent Publication Number WO 99/42447.

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[0037] Preferred compounds of formula (V) are:

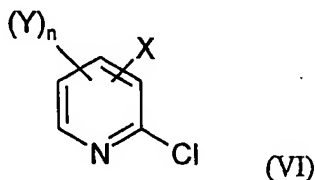
- \* N-[(3-chloro-5-trifluoromethyl-2-pyridyl)methyl]-2,6-dichlorobenzamide;
- \* N-[(3-chloro-5-trifluoromethyl-2-pyridyl)methyl]-2,6-difluorobenzamide;

- \* N-[(3-chloro-5-trifluoromethyl-2-pyridyl)methyl]-2-chloro-6-fluorobenzamide;
- \* N-[(3-chloro-5-trifluoromethyl-2-pyridyl)methyl]-2,3-difluorobenzamide;
- \* N-[(3-chloro-5-trifluoromethyl-2-pyridyl)methyl]-2,4,6-trifluorobenzamide or
- \* N-[(3-chloro-5-trifluoromethyl-2-pyridyl)methyl]-2-bromo-6-chlorobenzamide.

5

[0038] Process step (C) is described in International Patent Publication Number WO 99/42447.

[0039] According to a further feature of the invention the process (B), or the  
 10 combined processes (B) and (A), or (B), (A) and (C) can be combined with an earlier process step (D) which comprises the fluorination of a compound of formula (VI):



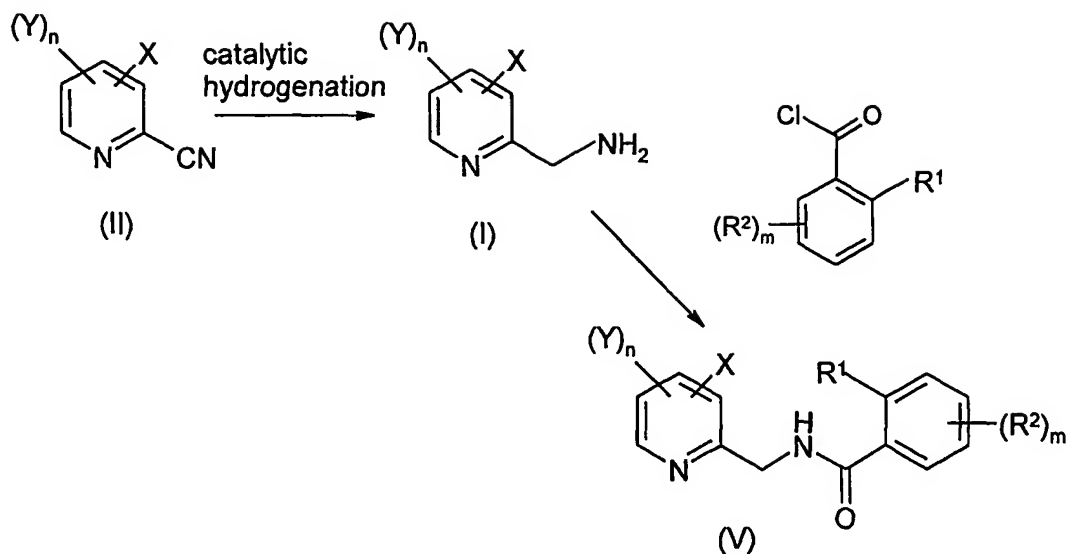
wherein X, Y and n are as defined above.

15

[0040] The process step (D) is generally performed using a suitable fluorinating agent such as an alkali metal fluoride, preferably potassium fluoride or sodium fluoride, in an aprotic solvent such as dimethyl sulfoxide or sulfolane, at a temperature of from 50°C to 150°C.

20

[0041] The compounds of formula (I) and (II) obtained by the above processes of the invention are particularly useful in the preparation of fungicidally active 2-pyridylmethylamine derivatives of formula (V), according to the following reaction scheme:



[0042] The present invention is further illustrated by the following preparative examples:

5 **Example 1 (Process step A)**

A mixture of 3-chloro-2-cyano-5-trifluoromethylpyridine (5.1 g) and 5% palladium on charcoal (5.1 mg as Pd metal) was stirred at 20°C with methanol and concentrated hydrochloric acid (2.5ml) under 1 atmosphere of hydrogen. After 4 hours the reaction was judged to be complete by hplc. The mixture was filtered  
 10 through Celatom, washed with methanol and water and evaporated to give 2-aminomethyl-3-chloro-5-trifluoromethylpyridine hydrochloride in 95-97% yield, NMR (in D<sub>2</sub>O) 4.6 (s, 2H), 8.35 (s, 1H), 8.9 (s, 1H).

**Example 2 (Process Step B)**

15 A solution of potassium cyanide (71.6g) in water (215g) was added during 1 hour to a stirred mixture of 3-chloro-2-fluoro-5-trifluoromethylpyridine (199.5g) and Aliquat 336 (tricaprylmethylammonium chloride, 12.1g) at 30°C. Stirring was maintained at this temperature for 4 hours at which time the amount of starting fluoride was less than 1% by hplc. The lower organic phase was separated and  
 20 washed with aqueous sodium chloride solution and distilled to give 3-chloro-2-

cyano-5-trifluoromethylpyridine (185.8g, 90% yield) bp 90°C at 15mbar. The purity of this product was 98%.

**Example 3 (Process Step B)**

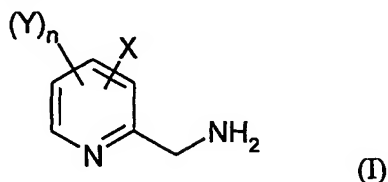
- 5 Solid sodium cyanide (0.29g) was added to a stirred mixture of 3-chloro-2-fluoro-5-trifluoromethylpyridine (0.8g) and tetrabutylammonium bromide (0.06g) at 20-25°C, and stirred for 23 hours to give 3-chloro-2-cyano-5-trifluoromethylpyridine (0.68g, 82% yield by hplc).

10 **Example of Process Step (D)**

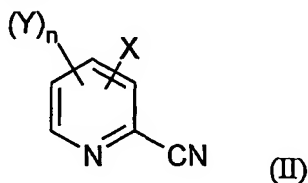
- 2,3-Dichloro-5-trifluoromethylpyridine (800g) was added to a stirred mixture of anhydrous potassium fluoride (320g) and anhydrous dimethylsulphoxide at 110°C then heated at 120°C for 2 hours and fractionally distilled under reduced pressure to give 3-chloro-2-fluoro-5-trifluoromethylpyridine (685g) in a yield of 92% (98%  
15 purity).

CLAIMS

1. A process for the preparation of a compound of general formula (I):



- 5 or a salt thereof, which process comprises the catalytic hydrogenation of a compound of general formula (II):



or a salt thereof,

wherein X is halogen; each Y, which may be the same or different, is halogen,

10 haloalkyl, alkoxycarbonyl or alkylsulphonyl; and n is 0 to 3.

2. A process according to claim 1 in which X is chlorine.
3. A process according to claim 1 or 2 in which Y is halogen or haloalkyl.
- 15 4. A process according to claim 3 in which Y is trifluoromethyl.
5. A process according to claims 1 to 4 in which the catalyst comprises a metal selected from palladium, platinum, ruthenium, nickel and cobalt.
- 20 6. A process according to claims 1 to 5 in which the catalyst is palladium.

7. A process according to claim 5 or 6 in which the amount of metal in the catalyst is from 0.05-0.7% by weight relative to the amount of the compound of formula (II).

5 8. A process according to claim 5 or 6 or 7 in which the amount of metal in the catalyst is from 0.05-0.3% by weight relative to the amount of the compound of formula (II).

9. A process according to claim 5 or 6 or 7 or 8 in which the amount of metal  
10 in the catalyst is from 0.1-0.2% by weight relative to the amount of the compound of formula (II).

10. A process according to any one of the preceding claims which is conducted in the presence of an alcohol solvent.

15

11. A process according to claim 10 in the alcohol solvent is methanol.

12. A process according to any one of the preceding claims which is performed at 0 to 60°C.

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13. A process according to any one of the preceding claims which is performed at a hydrogen pressure of from 1 to 4 atmospheres.

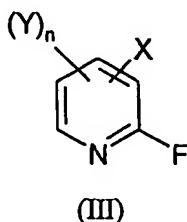
14. A process according to any one of the preceding claims which is  
25 performed in the presence of a catalyst inhibitor.

15. A process according to claim 14 in which the catalyst inhibitor is selected from an alkali metal bromide or iodide, ammonium bromide or iodide and hydrogen bromide or iodide.

30

16. A process according to any one of the preceding claims in which the compound of formula (II) is 3-chloro-2-cyano-5-trifluoromethylpyridine.

17. A process for the preparation of a compound of general formula (II) as  
5 defined in any one of claims 1 to 4, which process comprises treating a compound of general formula (III):



with a cyanide source and a catalyst in an aqueous solvent or without solvent,  
10 wherein:  
X, Y and n are as defined in claim 1; and wherein the cyanide source is hydrogen cyanide, an alkali metal cyanide, an alkaline earth metal cyanide or an optionally substituted ammonium cyanide.

15 18. A process according to claim 17 in which the catalyst is a phase transfer catalyst; or a crown ether or acyclic analogue thereof; or an amine.

19. A process according to claim 17 or 18 in which the catalyst is a tetraalkyl ammonium salt or a tetraalkyl phosphonium salt.

20

20. A process according to claim 17, 18 or 19 in which the catalyst is selected from tricaprylylmethylammonium chloride and tetra-n-octylammonium bromide.

21. A process according to any one of claims 17 to 20 in which the amount of  
25 catalyst used is from 0.01 to 10 mol %.

22. A process according to any one of claims 17 to 21 in which the cyanide source is potassium cyanide.

23. A process according to any one of claims 17 to 22 in which the amount of  
5 cyanide source used is from 1.0 to 2.0 molar equivalents.

24. A process according to any one of claims 17 to 23 in which the solvent is water.

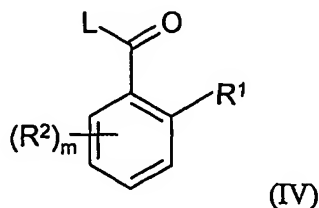
10 25. A process according to any one of claims 17 to 24 in which the temperature is from 10 to 60°C

26. A process according to any one of claims 17 to 25 in which the compound of formula (III) is 3-chloro-2-fluoro-5-trifluoromethylpyridine.

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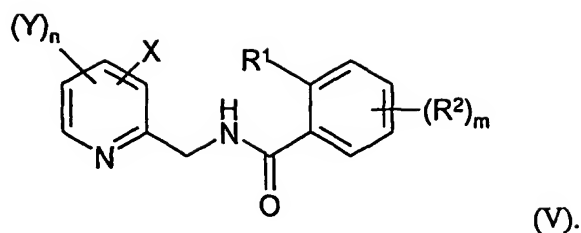
27. A process according to any one of claims 17 to 26, which is followed by a process according to any one of claims 1 to 16.

28. A process according to any one of claims 1 to 16 or 27, which is followed  
20 by a further process step which comprises the acylation of said compound (I) with a benzoyl compound of formula (IV):



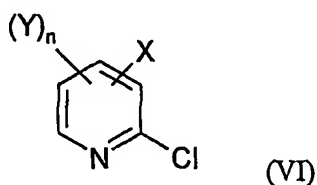
wherein L is a leaving group; R<sup>1</sup> and R<sup>2</sup> each represent the same or different halogen; and m is 0, 1 or 2, to give a compound of formula (V):





29. A process according to claim 17, 27 or 28 which is combined with an earlier process step which comprises the fluorination of a compound of formula

5 (VI):



wherein X, Y and n are as defined above.

30. A process according to any one of the preceding claims in which X is  
10 chlorine.

31. A compound of formula (I) when produced by a process as defined in any one of claims 1, 27 or 30.

15 32. A compound which is 2-aminomethyl-3-chloro-5-trifluoromethyl-pyridine hydrochloride.

33. A compound of formula (II) when produced by a process as defined in claim 17 or 29.

20

34. A compound of formula (V) when produced by a process as defined in claim 28 or 29.

35. A compound according to claim 34 which is:

N-[(3-chloro-5-trifluoromethyl-2-pyridyl)methyl]-2,6-dichlorobenzamide;

N-[(3-chloro-5-trifluoromethyl-2-pyridyl)methyl]-2,6-difluorobenzamide;

N-[(3-chloro-5-trifluoromethyl-2-pyridyl)methyl]-2-chloro-6-fluorobenzamide;

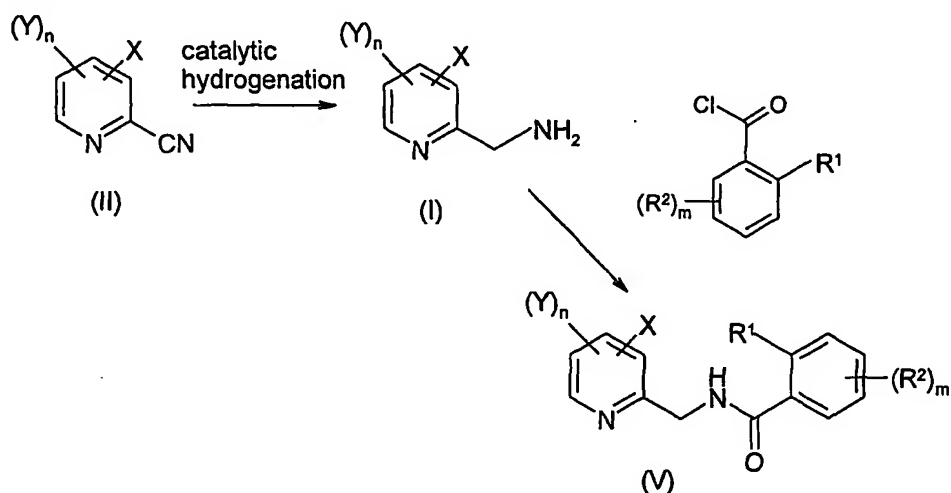
5 N-[(3-chloro-5-trifluoromethyl-2-pyridyl)methyl]-2,3-difluorobenzamide;

N-[(3-chloro-5-trifluoromethyl-2-pyridyl)methyl]-2,4,6-trifluorobenzamide or

N-[(3-chloro-5-trifluoromethyl-2-pyridyl)methyl]-2-bromo-6-chlorobenzamide.

36. A process for the preparation of compounds of formula (V), characterised

10 by the following scheme:



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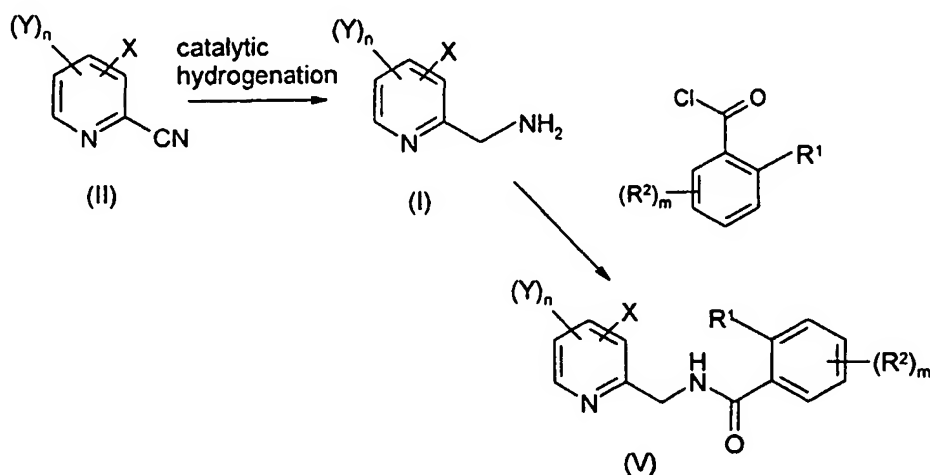
(43) International Publication Date  
28 February 2002 (28.02.2002)

PCT

(10) International Publication Number  
**WO 02/16322 A3**

- (51) International Patent Classification<sup>7</sup>: C07D 213/61. 213/26, 213/84
- (74) Agents: TETAZ, Franck et al.: Aventis CropScience S.A., Dépt. Propriété Industrielle, B.P. 9163, 14-20, rue Pierre Baizet, F-69263 Lyon Cedex 09 (FR).
- (21) International Application Number: PCT/EP01/10984
- (22) International Filing Date: 21 August 2001 (21.08.2001)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:  
0021066.6 25 August 2000 (25.08.2000) GB  
0025616.4 19 October 2000 (19.10.2000) GB  
01420128.9 7 June 2001 (07.06.2001) EP
- (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.
- (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- (71) Applicant (*for all designated States except US*): AVENTIS CROPSCIENCE SA [FR/FR]; 55, avenue René Cassin, F-69009 Lyon (FR).
- (72) Inventors; and
- (75) Inventors/Applicants (*for US only*): DANN, Norman [GB/GB]; Aventis CropScience UK Ltd, Hauxton, Cambridge CB2 5HU (GB). RIORDAN, Peter, Dominic [GB/GB]; 8 Counting House Lane, Dunmow, Essex CM6 1BX (GB). AMIN, Mehul, Rasikchandra [GB/GB]; 5 Betony Walk, Haverhill, Suffolk CB9 7YA (GB). MEL-LOR, Michael [GB/GB]; Aventis CropScience UK Ltd, Hauxton, Cambridge CB2 5HU (GB).
- Published:  
— with international search report
- (88) Date of publication of the international search report:  
6 June 2002
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: PROCESS FOR THE PREPARATION OF 2-AMINOETHYLPYRIDINES



(57) Abstract: The invention relates to a process for the preparation of a compound of formula (V), according to the following scheme: wherein the various substituents are as defined in the description.

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/EP 01/10984

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D213/61 C07D213/26 C07D213/84

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, PAJ, WPI Data, BIOSIS, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	EP 0 369 208 A (CL PHARMA) 23 May 1990 (1990-05-23) page 3, line 34 - line 51; example 1 ---	1-16, 27-30, 36
Y	EP 0 535 518 A (HOECHST AG) 7 April 1993 (1993-04-07) page 2; example 1a ---	1-16, 27-30, 36
Y	DATABASE WPI Week 198651 Derwent Publications Ltd., London, GB; AN 1986-336001 XP002189143 & JP 61 251663 A (KOEI CHEM. IND. CO. LTD.), 8 November 1986 (1986-11-08) abstract --- -/--	1-16, 27-30, 36

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
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- \*O\* document referring to an oral disclosure, use, exhibition or other means
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- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*&\* document member of the same patent family

Date of the actual completion of the international search

5 February 2002

Date of mailing of the international search report

20/02/2002

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# INTERNATIONAL SEARCH REPORT

Int. .tional Application No

PCT/EP 01/10984

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 4 159 382 A (GARROU PHILIP E) 26 June 1979 (1979-06-26) the whole document ---	1-16, 27-30, 36
Y	US 4 851 539 A (JOHNSTON HOWARD ET AL) 25 July 1989 (1989-07-25) column 7; example 1 ---	17-30, 36
Y	US 4 766 219 A (ORVIK JON A ET AL) 23 August 1988 (1988-08-23) column 2 -column 3 column 4 -column 5 ---	17-30, 36
A	---	29
Y	WO 92 18487 A (ICI PLC) 29 October 1992 (1992-10-29) page 51; example 6 ---	17-30, 36
Y	EP 0 034 917 A (ISHIHARA MINING & CHEMICAL CO) 2 September 1981 (1981-09-02) cited in the application preparation examples 3 and 4 ---	17-30, 36
X	WO 99 42447 A (MOLONEY BRIAN ANTHONY ;SAVILLE STONES ELIZABETH ANNE (GB); AGREVO) 26 August 1999 (1999-08-26) cited in the application start. mat. ex. 4; cpds 14,21,27,31,32 example 1 -----	32, 35
Y	---	28-30, 36

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 01/10984

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0369208	A	23-05-1990	AT 391693 B 12-11-1990
			AT 278988 A 15-05-1990
			AT 86978 T 15-04-1993
			AU 628100 B2 10-09-1992
			AU 4465789 A 24-05-1990
			CA 2002757 A1 15-05-1990
			CN 1042705 A 06-06-1990
			CS 8906438 A3 15-01-1992
			DD 284877 A5 28-11-1990
			DE 3840372 A1 31-05-1990
			DE 58903808 D1 22-04-1993
			DK 568989 A 16-05-1990
			EP 0369208 A1 23-05-1990
			ES 2053906 T3 01-08-1994
			GR 3007391 T3 30-07-1993
			HU 52480 A2 28-07-1990
			IL 92152 A 13-05-1993
			JP 2180868 A 13-07-1990
			NO 894410 A 16-05-1990
			NZ 231252 A 28-05-1991
			PH 25813 A 05-11-1991
			PT 92307 A , B 31-05-1990
			SU 1745121 A3 29-06-1992
			US 5066810 A 19-11-1991
			YU 216389 A1 28-02-1991
			ZA 8908273 A 25-07-1990
EP 0535518	A	07-04-1993	DE 4132808 A1 08-04-1993
			CA 2079155 A1 03-04-1993
			DE 59205946 D1 15-05-1996
			EP 0535518 A1 07-04-1993
			ES 2087387 T3 16-07-1996
			US 5374728 A 20-12-1994
JP 61251663	A	08-11-1986	JP 1877200 C 07-10-1994
			JP 6000749 B 05-01-1994
US 4159382	A	26-06-1979	NONE
US 4851539	A	25-07-1989	US 4565568 A 21-01-1986
			AT 33387 T 15-04-1988
			AU 556172 B2 23-10-1986
			AU 1533483 A 15-12-1983
			BR 8303329 A 07-02-1984
			CA 1179350 A1 11-12-1984
			CA 1182459 A2 12-02-1985
			DE 3376211 D1 11-05-1988
			DK 281183 A , B, 19-12-1983
			EG 17924 A 30-08-1991
			EP 0097460 A1 04-01-1984
			ES 523398 D0 01-10-1984
			ES 8500236 A1 01-01-1985
			ES 530712 D0 16-05-1985
			ES 8505346 A1 01-09-1985
			ES 530713 D0 01-05-1985
			ES 8504716 A1 16-07-1985
			GB 2123819 A , B 08-02-1984
			GR 79319 A1 22-10-1984

# INTERNATIONAL SEARCH REPORT

Information on patent family members

Int. l.ional Application No

PCT/EP 01/10984

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 4851539	A	IL 68822 A	12-07-1990
		JP 1439635 C	19-05-1988
		JP 59007165 A	14-01-1984
		JP 62049269 B	19-10-1987
		JP 62142156 A	25-06-1987
		JP 62142154 A	25-06-1987
		JP 62142157 A	25-06-1987
		KE 3734 A	19-06-1987
		KR 9005134 B1	20-07-1990
		MY 28087 A	31-12-1987
		NZ 204629 A	08-10-1986
		PH 21942 A	15-04-1988
		US RE33478 E	11-12-1990
		US 4678509 A	07-07-1987
		ZA 8304462 A	27-02-1985
US 4766219	A	23-08-1988 YU 45286 A1	30-06-1988
WO 9218487	A	29-10-1992 AT 167476 T	15-07-1998
		AU 656958 B2	23-02-1995
		AU 1538092 A	17-11-1992
		BR 9205902 A	08-11-1994
		CA 2107084 A1	16-10-1992
		DE 69225970 D1	23-07-1998
		DE 69225970 T2	15-10-1998
		EP 0586393 A1	16-03-1994
		WO 9218487 A1	29-10-1992
		GB 2270075 A ,B	02-03-1994
		HU 67924 A2	23-03-1995
		JP 3112479 B2	27-11-2000
		JP 6507394 T	25-08-1994
		KR 225619 B1	15-10-1999
		NZ 242290 A	22-12-1994
		OA 9912 A	15-09-1994
		US 5439910 A	08-08-1995
EP 0034917	A	02-09-1981 JP 1487910 C	23-03-1989
		JP 56118065 A	16-09-1981
		JP 63038990 B	03-08-1988
		JP 1468879 C	30-11-1988
		JP 56118066 A	16-09-1981
		JP 63018587 B	19-04-1988
		DE 3165316 D1	13-09-1984
		EP 0034917 A1	02-09-1981
		US 4367336 A	04-01-1983
WO 9942447	A	26-08-1999 AU 2527199 A	06-09-1999
		BR 9908007 A	30-01-2001
		CN 1291187 T	11-04-2001
		CZ 20002993 A3	14-11-2001
		EP 1056723 A1	06-12-2000
		WO 9942447 A1	26-08-1999
		HU 0100817 A2	30-07-2001
		NO 20004159 A	17-10-2000
		PL 342376 A1	04-06-2001
		SI 20356 A	30-04-2001
		SK 12392000 A3	12-03-2001
		TR 200002395 T2	21-11-2000

## INTERNATIONAL SEARCH REPORT

### Information on patent family members

Int. \_lional Application No

PCT/EP 01/10984

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9942447 A		ZA 9901292 A	13-09-1999